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Original Research Article

A Cross Sectional Study on Platelet Indices in Acute Ischemic Stroke among Adults in a Tertiary Care Hospital

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Abstract

Aim of the Study: To investigate relationship between platelet indices, MPV (mean platelet volume) and PDW (platelet distribution width) in acute ischemic stroke.

Methods:80 stroke patients admitted to the hospital from November 2018 to October 2020 were screened. Each of them was entered into a stroke log. Patients fulfilling the criteria were enrolled into the study after obtaining an informed consent. Each patient was given a serial number and was formally included into the study as a case.

Results: Age group with highest stroke incidence is 61-70yr, with 66.7% falling in the age group. 17.5% are between 51- 60yrs age group. 11.3% for 71-80 yrs, and 5% are stroke in young. 66.3% of the cases were males and 33.8% are females. There was a clear male preponderance in the cases of stroke recruited in this study.

Conclusion: The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required into the role of platelet volume in stroke pathology, outcome, and, most importantly, in individuals at risk for stroke.

Keywords: Mean Platelet Volume (MPV); Platelet distribution width (PDW); ischemic Stroke.

Introduction

Cerebrovascular diseases include some of the most common and Devastating disorders Stroke is one of the major causes of human morbidity and mortality. It ranked as the sixth leading cause of disability- Adjusted years (DALY; one DALY is one of the lost years of healthy life) Stroke is associated with increased long term mortality, residual Physical, cognitive, and behavioural impairments, recurrence, and increased risk of other types of vascular events Prevalence of stroke ranges from 84–262/100,000 in the rural Setting and from 334–424/100,000 in the urban areas in India. The Incidence is about 119–145/100,000 based on recent population-based studies. Among them, 80% are ischemic stroke, and Haemorrhagic stroke make up the remainder [1].

Several factors are known to increase the liability to stroke. The most important of these are hypertension, heart disease, atrial fibrillation, diabetes mellitus, cigarette smoking, and hyperlipidemia [2]. Platelet size is also found to be elevated in individuals with hypertension and diabetes mellitus [3]. both conditions that predispose to the development of vascular disease [4]. Since this is such a huge public health problem, other risk factors and possible preventive measures need to be identified. It is in this context that this study has its significance.

Though there have been quite a few studies which have demonstrated an association between myocardial infarction and platelet size, very few studies have looked at the association between platelet size and ischemic stroke hence an attempt has been made to study the association if any between mean platelet volume and stroke in an Indian population. And establishing relation between the platelet indices and stroke will helps in better screening of the disease and it's prevention.

Aims of the study

To investigate relationship between platelet indices, MPV (mean platelet volume) and PDW (platelet distribution width) in acute ischemic stroke.

MPV and PDW are different for each laboratory depending on the coulter used. And ranges also vary depending on the preservative used in the vaccutainer. So, it's important to determine the normal range of the desired values at the institution of study.

Platelet indices can also be compared with carotid stenosis, Hba1c levels, blood sugars, or any other organ dysfunctions, so that the cumulative risk can be calculated. It has been tried in the secondary outcomes of the study. Future studies can target multiple factors along with platelet indices so, association and risk can be assessed with better confidence intervals

Materials and Methods

80 patients of this study admitted in Tertiary Care hospital which is a tertiary care Hospital Hyderabad, Telangana State.

Inclusion Criteria:

- History and physical examination suggestive of Acute Ischemic Stroke.
- Imaging proven Acute Ischemic Stroke

Definition of stroke: Focal neurological deficit lasting more than 24hrs with no evidence of a non – vascular cause

Exclusion Criteria:

- Age < 18years.
- Hemorrhagic stroke.
- Comorbidities like liver failure, Chronic Kidney Disease (CKD), Congestive cardiac failure (CCF).
- Recent episode of infections.
- Previous history of stroke, Transient ischemic attack (TIA), Peripheral Vascular disease (PVD).
- Patients on antiplatelet drugs and immunosuppressants

Sysmex Coulter:

It works on the principle of electrical impedance method. The aspirated sample enters the metering unit after 2 times dilution. The little opening on the metering unit is called aperture. A pair of electrodes are positioned on both sides of aperture to create a constant current supply. As cells are poor conductors when each particle in the diluted sample passes through the aperture a transitory change in direct current resistance between the electrodes is produced, this produces a measurable electrical pulse which is proportional to size of the particle. The number of pulses indicates number of particles.

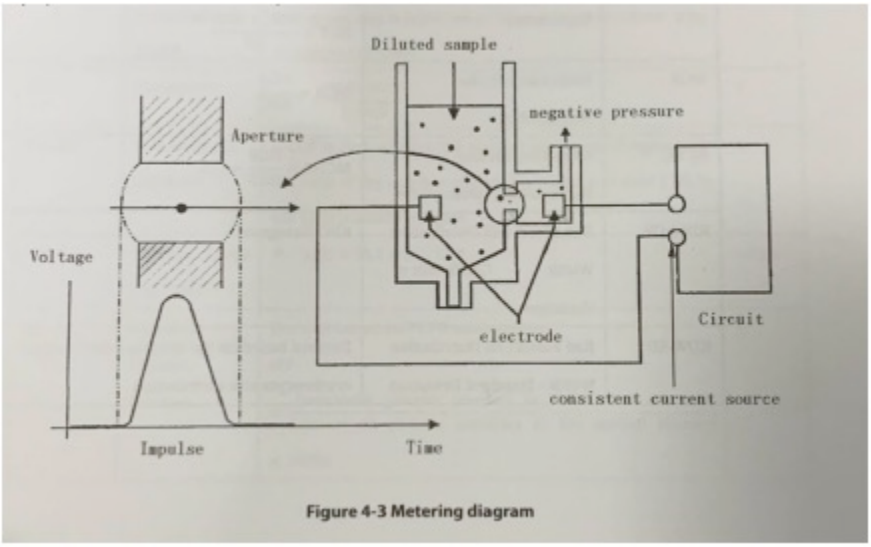

Figure 4-3 Metering diagram

Results

Table 1: Distribution of type of stroke

Diagnosis	Frequency	Percentage
AIS, CVA Left Hemiparesis	42	52.5%
AIS, CVA Right hemiparesis	38	47.5%
Total	80	100%

Table 2: Depicting territory of involvement according to CT brain findings

Territory involved on CT Brain	Frequency	Percentage
CG Region	43	5.8%
Corona Radiata	6	7.5%
MCA	25	31.3%
PCA	6	7.5%
Total	80	100%

Table 3: Depicting the relation between MPV, PDW and platelet count.

MPV Categories								
	1		2		3		Total	
	MEAN	Standard	MEAN	Standard	MEAN	Standard	MEAN	Standard
MPV	8.1	2	9.5	4	10.3	0.4	9.7	0.7
PDW	15.4	6	15.7	5	16.3	0.5	15.9	0.6
PC	2.9	1.0	3.1	9	3.2	0.8	3.1	0.9

Table 4: Depicts cranial nerve involvement in right and Left hemiparesis

Special features	AIS CVA Left Hemiparesis		AIS CVA Right Hemaparesis	
	Frequency	Percentage	Frequency	Percentage
No	30	37.5%	20	25.0%
7^{th}	10	12.5%	16	20.0%
Lower Cranial Nerve	2	2.5%	2	2.5%

Table 5: Shows the relationship between haemoglobin, creatinine and urea

MPV Categories								
	1		**2**		**3**		**Total**	
	MEAN	Standard	MEAN	Standard	MEAN	Standard	MEAN	Standard
HB	12.0	0.8	11.3	1.2	11.5	1.1	11.5	1.2
CREAT	1.3	0.9	1.1	0.4	1.1	0.4	1.1	0.5
UREA	29	20	24	8	22	11	24	10

Table 6: Shows the relationship between triglycerides, LDL & HDL

Categories								
	1		**2**		**3**		**Total**	
	MEAN	Standard	MEAN	Standard	MEAN	Standard	MEAN	Standard
TG	268	53	221	52	217	51	223	53
LDL	157	30	143	25	153	23	149	25
HDL	29	8	30	5	29	5	29	5

Table 7: Depicts the relation between MPV and 2DECHO findings

MPV	**2D Echo Ejection fraction**	
1	Mean	49
	Standard Deviation	6
2	Mean	53
	Standard Deviation	6
3	Mean	52
	Standard Deviation	7
Total	Mean	52
	Standard Deviation	7

Table 8: Depicts the relation between MPV and serum electrolytes

MPV		**Sodium**			**Potassium**	
		High	**Low**	**Normal**	**Low**	**Normal**
1	N	0	2	4	0	6
	N%	0.0%	2.5%	5.0%	0.0%	7.5%
2	N	1	2	38	1	40
	N%	1.3%	2.5%	47.5%	1.3%	50.0%
3	N	2	2	29	0	33
	N%	2.5%	2.5%	36.3%	0.0%	41.3%
Total	N%	3.8%	7.5%	88.8%	1.3%	98.8%
CHI SQUARE P VALE		0.1			0.6	

Discussion

Previous studies have documented various platelet abnormalities in cerebrovascular disease.eg, circulating platelet aggregates, platelet aggregation, and increased release of platelet-specific α granule proteins, thereby indicating platelet activation. Others have shown that platelet aggregation is not increased in the acute phase but occurs several days after the event. This lack of detectable activation in the acute phase has been attributed to platelet consumption during the event. However, the lack of agreement between these studies may relate

to specimen handling and different methodology.

Platelet parameters and stroke

Platelet parameters assessed were MPV, PDW, and Platelet count. The main parameter studied was MPV. MPV has got a statistically significant correlation with ischemic stroke with a p value of <0.01 with an average MPV in cases being 9.7 with SD 0.7 compared to controls who average 6.94±0.59, though the method of analysis and the principle of analyser have different values.

MPV assessment using EDTA and Citrate has been done only in one other study i.e. Butter worth *et al* and the values were 8.04±1.04 (7.69±0.83) for EDTA and 7.35± 1.05(7.09±0.74) for citrate. The values were comparable even though these studies have been done in different populations. All the other studies have used EDTA as the anticoagulant and there is no uniformity in the collection method, time of analysis, transport of the specimen or the storage. O'Malley *et al* [5] study has performed the test after 24hrs of storage in room temperature. Most of the other studies have performed the test after 2hrs. In this study the samples were analysed after 2 hrs of storage in room temperature. The only study with a lower MPV in cases compared to controls is Tohji *et al* [6] This study did not specify the time after venipuncture at which samples were analysed or temperature at which it was stored.

In the current study the platelet count 3.1 lakh with SD of 0.9 lakh. This trend is however not statistically significant. This pattern has been seen in all the other case control studies which included O'Malley *et al*, Butterworth *et al* [7] and Tohji *et al*.

It has been suggested that MPV and platelet count are under independent hormonal control, although control of platelet production remains obscure. Some have suggested a role for interleukin-6, interleukin-3, thrombopoietin, and colony-stimulating factors. It is, however, generally accepted that platelet volume and count are determined at thrombopoiesis, and as in ischemic heart disease, these findings may implicate primary changes occurring at the bone marrow (megakaryocyte) level. Moreover, an increase in megakaryocyte size and ploidy (DNA content) coincides with an increase in MPV. This direct association suggests the possibility that activation of megakaryocytes, as heralded by an increase in MPV, is a feature of ischemic stroke.

Mean PDW is 15.9 with SD 0.6. Highest PDW is associated with the MPV range of 10-12 with a mean of 16.3 and standard deviation of 0.5. PDW has a narrow range of 16-18 for the analyser used for the study and variation of 10-18% is normal. PDW is proportionately related to MPV in healthy individuals, though not completely this helps in assessing whether the patient has any predisposed platelet disorders. However, in non-physiological conditions it may vary as in threatened preterm labour causes significant dissonance - a raise in PDW associated with decreased MPV observed by Aydogan *et al*. In this study, high MPV is associated with high PDW.

In relation to age PDW is highest among oldage people with mean being 16 with SD 0.5 for 51 – 60 yrs, mean 15.9 SD 0.6 for 61 – 70 yrs., mean 16 with SD 0.6. Among younger individuals with age less than 50 years the PDW is 15.5 with SD 0.3. Stroke in young got less correlation with PDW whereas older people got greater correlation with high PDW. Mean PDW among male population is mean 16 with SD of 0.5 whereas in females it is 15.8 with SD 0.7.

PDW in relation to region involved on CT brain has a very little variation. Mean PDW

of 15.9 for CG region and PCA stroke and 16 for MCA and corona radiata.

Mean ejection fraction of the cases admitted is 52%, with no big difference among the three MPV categories. Most of the patients are not with heart failure, as patients on antiplatelets are in the exclusion criteria for the study. And MPV has no association with heart functioning in the study. However, some previous studies have found out, high MPV is associated with Acute Coronary Syndromes

25 out of 80 patients are having carotid stenosis >70%. Out of these 24 of the patients have MPV greater than 8.5, indicating patients with greater stenosis have higher risk of CVA if MPV is high.

47.5% cases have have stenosis less than 30%. They didn't show any significant association with high MPV in regards to CVA. All the cases with established liver disorders is among exclusion criteria for this study. Mean of ALT is 30, and mean of AST is 35, and liver enzymes got no correlation with MPV and stroke in this study.

Comparison of platelet parameters of the current study with western literature

MPV with EDTA has similar range in many western studies, and its association with acute ischemic stroke also has similar correlation.

The Oxfordshire community stroke project classification of stroke syndromes was used to classify strokes into Lacunar and Non-Lacunar Syndromes (PACS, POCS and TACS). Two studies i.e. Butterworth *et al* and A. Muscari *et al* [8] found statistically significant increase of MPV in Non Lacunar strokes when compared to Lacunar strokes. However O'Malley *et al* did not find any such correlation. Similarly in this study no statistically significant correlation has been established. This study confirms that patients with ischaemic stroke have larger platelets a finding that is compatible with other reports of accentuated platelet function in brain infarction, including elevated blood and urine levels of b - thromboglobulin (b -TG) and TxA2. However, we have not been able to establish that thrombomegaly is restricted to patients with cortical ischaemic stroke. Cortical events are usually related to atherothromboembolic events that occur in the heart, aorta, carotid arteries or large intracranial arteries are likely to involve platelet activation.

Conversely, many deep white matter lacunar strokes are considered to be a consequence of small vessel lipohyalinosis, a disease process not involving platelets46.

A similar study was conducted by Griesenegger *et al* and an increased MPV was associated with a worse outcome in patients suffering an acute ischemic cerebrovascular event. Patients within the highest quintile of MPV had a 2-fold risk of suffering a severe stroke compared with patients within the lowest quintile. The association of high MPV with severe stroke remained significant after adjustment for confounding factors. The p value was 0.002 in this particular study. In our study the cases were recruited from medical and wards and though there were intensive treatment units, patients who needed ventilatory support were admitted to the intensive care unit and such patients were not included. This would have lead to a bias since seriously ill patients were not recruited.

Indian scenario, study conducted by Department of Medicine, Medical College, Kolkata, West Bengaltitled, 'Platelet Indices as a Marker of Severity in Non-diabetic Non-Hypertensive Acute Ischemic Stroke Patients' concluded that in patients of ischemic stroke platelet indices may be used for predicting severity of motor deficit. Although larger sample size and multivariate analysis is required before this can be used regularly in clinical practice which included

Pikija *et al* [9] Correlation coefficient between the values of motor deficit scores (based on CNS) and platelet indices of stroke patients were calculated. The severity of motor deficits was significantly correlated with the values of PDW ($r= 0.556$, $p<0.01$) and MPV ($r=-0.46$, $p<0.05$). Thus, patients with lower CNS scores for motor deficits (indicating more severe deficits) had higher mean platelet volumes and platelet distribution widths. Compared to this particular study severity of stroke is not studied. But association of high MPV with stroke is established with a P-value of <0.001.

Another study at ST. Jhons medical college, Bangalore on MPV and stroke concluded that, there is elevation of MPV in the acute phase of ischemic stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, it can be stated that an increase in MPV is independently associated with stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required into the role of platelet volume in stroke pathology, outcome, and, most importantly, in individuals at risk for stroke. Platelet mass was found to be more or less a constant.

No statistically significant correlation between clinical severity of stroke and mean platelet volume. Strokes were sub typed clinically and based on the vascular territory on MRI. However no statistical correlation was obtained when MPV was compared to the various subtypes of stroke. Thrombomegaly is restricted not just to patients with cortical ischaemic stroke but also with lacunar syndromes. However, contrast to this particular study, there strong correlation of MPV with CG region strokes, which is in line with many western studies.

Conclusion

1. In our study majority of stroke was caused in seventh decade of life, with 66.3% falling in the age group of 61-70. Stroke incidence was seen to be high in sixth decade when compared to eight decades of life, probably due to, low life expectancy. Stroke in young age
2. Present study included 53 males and 27 females. That is 66% being male and 34% being female. Hence there was a male predilection among subjects.
3. Cranial nerve involvement was seen in 37.5% cases, out of which only 5% had lower cranial nerve involvement, rest were associated with facial palsy
4. The CT findings of subjects in our study showed that CG region was involved in 53.8%, MCA in 31.3%, corona radiata and PCA involved in 7.5% each.
5. Most of the CVA patients in our study had MPV in the range of 8.5 to 12 that is 92.3 % strokes had higher MPV values. And among the subjects 41% had very high MPV, which was greater than 10.
6. Our cross-sectional study showed that the association between MPV and AIS was- P VALUE
7. P value for Mean PDW Vs Territory involved in brain was calculated to be 0.9, therefore no significant association found.

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